

The Combined Cognitive Bias Hypothesis in Depression:
A State-of-the-art

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Abstract

Drawing from substantial evidence demonstrating cognitive biases in depression at various stages of information processing (i.e., attention, interpretation, memory, cognitive control), we argue for an approach that considers the interplay among these processes. This paper attempts to apply the combined cognitive bias hypothesis (Hirsch, Mathews, & Clark, 2006) to depression research and reviews competing theoretical frameworks that have guided research in this area. We draw on current findings from behavioral studies on the interplay between depression-related processing biases. These data indicate that various cognitive biases are associated. However, it is not clear whether single or multiple biases are most predictive of depressive symptoms. We conclude this article with theoretical and clinical implications of the current state of research in this field and propose a number of ways in which research on the combined cognitive bias hypothesis can be advanced.

Keywords: combined cognitive biases, depression, attention, interpretation, memory, cognitive control

The Combined Cognitive Bias Hypothesis in Depression:

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Major depression is a prevalent psychiatric disorder that is associated with debilitating symptomatic suffering, functional impairments, and high societal costs (Kessler & Wang, 2009). Notwithstanding a range of well-established psychological and pharmacological interventions, relapse and recurrence rates of depression remain high (Vittengl, Clark, Dunn, & Jarrett, 2007) indicating that current therapies do not sufficiently address vulnerability factors for this burdensome disorder. Moreover, with each successive depressive episode the risk for recurrence increases (Boland & Keller, 2009), which points to an expanding vulnerability with multiple episodes. Hence, profound insight into the mechanisms involved in the etiology and maintenance of major depression seems essential in improving contemporary treatment options and the prevention of depression.

In the past three decades, research inspired by cognitive accounts of depression has been successful in identifying vulnerability factors for this disorder. Apart from substantial research examining depressive *cognitive content* as a vulnerability factor (e.g., negative thoughts), a promising line of research highlights the role of *cognitive biases* in the development, maintenance, and relapse/recurrence of depression (for reviews see Gotlib & Joormann, 2010; Mathews & MacLeod, 2005). Research efforts in this particular area of interest have typically focused on abnormalities in attention, interpretation, and memory processes, which are considered to be instrumental in the understanding of the processes involved in these cognitive biases. More recently, there is growing interest into cognitive and neural mechanisms underlying cognitive control impairments, which may operate across a variety of cognitive biases. Indeed a substantial number of studies on emotional information processing in depressed samples provide evidence that depression is characterized by attention, interpretation, and memory biases, especially for negative information (see below).

This research has been guided by comprehensive cognitive frameworks of depression (e.g., D. A. Clark, Beck, & Alford, 1999; Ingram, 1984; Williams, Watts, MacLeod, & Mathews, 1988, 1997) and findings have led to the development of specific cognitive science approaches to depression (e.g., Holmes, Lang, & DePrese, 2009; Joormann, Yoon, & Zetsche, 2007).

Cognitive Biases and Vulnerability for Depression

What are, in broad terms, the findings on biased information processing in depression?¹ A recent meta-analysis showed that depressed samples (i.e., encompassing dysphoric, clinically depressed, and remitted depressed individuals) exhibit an attention bias favoring negative information and also an absence of a positivity bias, compared with nondepressed samples (Peckham, McHugh, & Otto, 2010). Specifically, selective attention for negative information is characterized by impaired disengagement of attention from the processing of negative information rather than enhanced engagement with negative information (De Raedt & Koster, 2010). At the level of interpretation processes, dysphoric and depressed individuals display a tendency to interpret emotionally ambiguous information in a negative manner. Current findings suggest that ambiguity resolution is distorted in the effortful generation of interpretations and the selection of a single interpretation as most likely applicable to an ambiguous situation (Wisco & Nolen-Hoeksema, 2010). Concerning memory processes, strong evidence exists that depression is marked by biases in explicit memory, with depressed individuals reporting overgeneral and more negative memories than specific and positive memories compared with nondepressed individuals (Matt, Vazquez, & Campbell, 1992; Williams et al., 2007). In contrast, the data from studies examining mood-congruent implicit memory biases in depression is less conclusive (Barry, Naus, & Rehm, 2004; P. C. Watkins, 2002). This bias might be observed only when there is a congruency between the depth of processing (e.g., perceptual, conceptual) at encoding and retrieval (Phillips, Hine, &

Thorsteinsson, 2010). Recent evidence points towards cognitive control impairments in depressed samples. In this respect, depressed individuals have shown difficulties in the inhibition of negative information (Goeleven, De Raedt, Baert, & Koster, 2006; Joormann, 2004), as well as in the processes involved in shifting and the updating of emotional and non-emotional representations in working memory (De Lissnyder et al., 2011; Lo & Allen, 2011).

Importantly, longitudinal studies and cognitive bias modification (CBM) research (i.e., experimental manipulation of processing biases) have shown that cognitive control deficits (Siegle, Ghinassi, & Thase, 2007; Zetsche & Joormann, 2011), biases in attention (Beevers & Carver, 2003; Wells & Beevers, 2010), interpretation (Blackwell & Holmes, 2010; Holmes, Lang, & Shah, 2009; Rude, Valdez, Odom, & Ebrahimi, 2003; Rude, Wenzlaff, Gibbs, Vane, & Whitney, 2002), and memory processes (Johnson, Joormann, & Gotlib, 2007; Raes, Williams, & Hermans, 2009; Sumner, Griffith, & Mineka, 2010) can predict and contribute to the onset and maintenance of depressive symptoms. Moreover, these distorted cognitive processes can be found in at-risk (Dearing & Gotlib, 2009; Joormann, Talbot, & Gotlib, 2007; Kujawa et al., 2011; Taylor & Ingram, 1999) and remitted (Fritzsche et al., 2010; Gilboa & Gotlib, 1997; Hedlund & Rude, 1995; Joormann & Gotlib, 2007, 2010) depressed samples. Taken together, an accumulative wealth of data yield evidence for cognitive biases operating at various stages of information processing in depression and demonstrate that these distorted cognitive processes are not merely mood-dependent correlates of the disorder.

Interrelations among Cognitive Biases

A key limitation of current research is that cognitive biases in depression have been mostly studied in isolation, and at rather specific stages of information processing. While this approach has some advantage in enhancing our understanding of how a specific cognitive bias affects behavior, it is limited in that it does not inform on how cognitive biases are associated and linked to higher-order factors (such as negative schema's, see below). Moreover, the

current focus on single biases provides a rather restricted understanding of the relative importance of how various biases may collectively influence the etiology and maintenance of depression. In other words, an integrated understanding of how cognitive biases act in concert can be achieved by investigating the interplay among biased attention, interpretation, and memory processes as well as cognitive control impairments.

This review applies the *combined cognitive bias hypothesis* (Hirsch, Clark, & Mathews, 2006) to the study of depression. We attempt to frame how cognitive biases operate in concert and subsequently elaborate upon the main empirical questions arising from the combined cognitive hypothesis. We follow by discussing predictions from key theoretical frameworks that can inform upon the interplay among cognitive biases, guiding future research in this area. We draw upon empirical studies that have directly examined links between multiple cognitive biases. We conclude this article with theoretical and clinical implications of the current findings and propose a number of ways in which this new area of research can be taken forward.

The Combined Cognitive Bias Hypothesis

Although many cognitive (-behavioral) models of psychopathology assume that cognitive biases should work in concert, their take on this assumption has been relatively limited (see the section on theoretical frameworks). It is only recently that specific ideas and hypotheses regarding the interplay between distorted cognitive processes in emotional disorders have begun to emerge in experimental psychopathology research (e.g., Hertel, 2004). In a paper focusing on bidirectional relations between interpretation biases and imagery, Hirsch et al. (2006) elaborated upon the notion of distorted cognitive processes working in concert and formulated the *combined cognitive bias hypothesis* (CCBH). It was argued that “cognitive biases do not operate in isolation, but rather can influence each other and/or can interact so that the impact of each on another variable is influenced by the other.

Via both these mechanisms we argue that combinations of biases have a greater impact on disorders than if individual cognitive processes acted in isolation” (p. 224). Although Hirsch and colleagues focused on cognitive processes in social anxiety disorder, the CCBH can equally be applied to other emotional disorders.

The past years have seen an accumulative number of studies directly examining interrelations among cognitive biases in dysphoric and clinical depression (see the section on empirical data). As this research is still in its infancy, several questions that require further empirical investigation remain. We have identified three broad types of questions originating from the CCBH, namely association, causal, and predictive magnitude questions. Table 1 provides a summary of the key issues within each type of questions.

Association Questions

The first type concerns what we refer to as “*association questions*”. These research questions address whether cognitive control impairments and biases at the levels of attention, interpretation, and memory are interrelated. Although several studies drawing from “association questions” (e.g., “are negative attention biases associated with enhanced memory for similar information?”) have been published (see the section on empirical data) many potential links have not been systematically explored. For example, no published research reports data on the association between biased attention and interpretation processes in depression, though influential cognitive models (e.g. Beck’s schema theory; see below) assume that there is a link. Clearly, findings from studies examining the “association questions” can provide a broad idea about various links among multiple distorted cognitive processes.

Causal Questions

Detailed insight into the functional interplay among cognitive biases is gained by studies that consider “*causal questions*”. Specific hypothesized causal relations among

different cognitive biases are the subject of this type of research questions. Two issues that deserve empirical consideration can be delineated. First, it is unclear whether multiple distorted cognitive processes operate in succession (i.e., unidirectional effects) with different processes influencing each other or, in contrast, operate in parallel without mutual influences. It could be, for instance, that an initial bias at encoding (e.g., attention bias) can influence subsequent biases (e.g., memory bias). Alternatively, these cognitive biases may operate simultaneously but independently from each other. In this instance, the extent to which cognitive biases are distorted may be influenced by other variables such as levels of depressive symptom severity.

A second major idea within the type of the “causal questions” that has largely gone untested is whether there are reciprocal relations between different biases. For example, it may be that negative attention biases (e.g., a critical remark of a loved one) lead to negative interpretations of the attended material (e.g., “she/he does not love me anymore”). Negative interpretations can in turn enhance attention to similar material (e.g., other signs of disapproval) and refine or strengthen the depressed person’s interpretations (e.g., “he/she hates me”).

In investigating the association and causal questions, it is important to consider whether the interplay among distorted cognitive processes has differential effects depending on the time course in depression severity (i.e., non-depressed at-risk, subclinical, clinical, and remitted depression). As we discuss later, the strength of processing abnormalities may partially depend on the level of depression severity, suggesting that the interplay between biased cognitive processes might not be static over time, but could change across stages and during the course of multiple depressive episodes. This warrants research scrutinizing association and causal questions in at-risk, currently, and remitted depressed samples.

Predictive Magnitude Questions

While the first two types of questions concern mutual relations among information processing biases within specific situations (proximal timeframes), “*predictive magnitude questions*” address the influences of single versus multiple cognitive biases on the course of depression mainly using prospective research designs (distal timeframe). Specifically, additive versus interactive effects that may extend beyond the effects of isolated cognitive biases on depressive symptoms are considered. At present, it remains unclear whether depressive symptoms are exacerbated or maintained by single or multiple cognitive biases, and whether having multiple biases has additive effects on depressive symptoms. Moreover, it is also possible that certain interactions between biases have potentially strong effects on depressive symptoms. For instance, in some models of depression it is argued that self-focused attention and memory bias are highly likely to have detrimental effects on depressed mood. Such questions are important in understanding the risk factors associated with depression, given that multiple vulnerability factors can increase the probability of developing a disorder, whereas an individual bias may not. That is, the predictive value of biases in isolation is often small to moderate and it could be that multiple cognitive biases and their interactive effects may have a stronger effect on the prediction of depression.

As argued in the context of each type of questions, we propose that instead of merely examining biases in isolation, multiple cognitive biases need to be taken into consideration. Later in this article, we will review the state-of-the-art of empirical research for each type of CCBH questions. We consider first theoretical predictions on the CCBH in depression, as they are crucial to guide empirical research in this area.

Cognitive Frameworks of Depression

In several conceptual frameworks of depression, cognitive biases are considered important in the etiology and maintenance of depressive symptoms. Below we briefly describe the most influential cognitive frameworks with their shared and unique predictions

with respect to the different types of CCBH questions.² Figure 1 depicts a schematic outline of the distinct cognitive frameworks.

Beck's Schema Model

One of the earliest models that has attributed a critical role to cognitive biases is Beck's schema theory (Beck, 2008; D. A. Clark et al., 1999). This theory states that depression-prone individuals hold negative schemata, which are dysfunctional mental representations about the self (i.e., on themes of personal loss, failure, or deprivation) and are developed in response to childhood experiences. When activated by stressful life events, negative schemata produce congruent biases in attention, interpretation, and memory for self-relevant information. For instance, a student with a history of failing oral exams (e.g., schema of failure) may be more attentive for social cues of disapproval displayed in the nonverbal behavior of an examiner (e.g., frowned eyebrows) during new exams. The student may interpret such facial expressions as a sign of disapproval (e.g., "I must have given a stupid answer") and recall negative memories about past failures (e.g., memories about the previous times failing an exam). Beck's formulation with cognitive schemas biasing information processing implies that cognitive processes (and biases) can occur interactively and concurrently at the automatic and strategic levels of processing (p. 58, D. A. Clark et al., 1999). This formulation is relevant for the "association questions" of the CCBH. Yet, the theory fails to provide a detailed account of testable predictions on causal relations among biased cognitive processes and it does not elaborate on interplay between automatic and strategic levels of information processing. Regarding differences in the interplay among different stadia of depression, the schema theory asserts that the magnitude of biases in attention, interpretation, and memory is a linear function of depressive symptom severity (pp. 168, 179; D. A. Clark et al., 1999). It is hypothesized that, as depressive symptoms develop, a

cognitive shift occurs from a positivity bias to facilitate the processing of negative information in clinically depressed individuals.

Whereas Beck's cognitive model predicts biases at all levels (i.e., automatic, strategic processing levels) and facets (i.e., attention, interpretation, memory biases) of information processing, other cognitive theorists, such as Ingram (1984) and Williams, Watts, MacLeod, and Mathews (1988, 1997), have proposed a more specific account of cognitive biases in depression. These theories are discussed in turn.

Enhanced Elaboration Accounts

Ingram's information processing analysis. Ingram (1984) attributes a crucial role to biased elaboration and memory in the maintenance of depression (association question). It is hypothesized that when depressive memory networks are activated by appraisals of life events, individuals elaborate extensively upon information that is congruent with the triggered negative cognitions. In keeping with the previous example, a student may appraise nonverbal cues, such as frowned eyebrows and crossed arms, as signs of failure (e.g., "my answer is not correct") which may activate corresponding depression networks resulting in a thorough evaluation of the attributes and implications of the situation (e.g., "I did not understand the lessons that well, I will not pass the exam, I am stupid"). This selective processing style can activate connected memory networks by associative linkages. These networks may contain, for example, negative cognitions that are related to past feelings of depression (e.g., "I screwed up my romantic relationships, I am a loser"). Activation of such connected networks in turn maintains biased elaboration on negative material (causal question). As a result of this process of recycling of negative cognitions through various memory networks, the elaborated material is encoded more deeply into the depressive memory networks increasing the chances that this negative memory content becomes activated in the future. This biased elaboration-

memory interaction heightens the vulnerability for depression and predicts future depressive episodes (predictive magnitude question).

Williams et al.'s cognitive framework. In their influential 1988 (and revised 1997) framework, Williams et al. argued that depression is characterized by negative biases in elaboration and not in priming processes of attention and memory (association question). Priming refers to automatic processes involved in strengthening representations making them more accessible, while elaboration refers to strategic processes which form or strengthen relations between activated representations (Graf & Mandler, 1984). Two mechanisms are proposed that underlie these negative biases, namely the affective decision mechanism (ADM) and the resource allocation mechanism (RAM). When the valence of incoming information is considered as negative (e.g., frowned eyebrows in the previous example), as assessed by the ADM, more attention resources are allocated to negative material (e.g., the examiner rolling his eyes, crossed arms) leading to enhanced elaboration (RAM). The student might think, for example, "I must have given a wrong answer, he/she must think that I am stupid, I am not capable of succeeding for the course". These depression-related elaborations are encoded into memory, enhancing later memory for depression-related material (causal question). Some predictions about the attention-memory interplay put forward in the 1988 model were revised in 1997. Based on the empirical data available, Williams et al. concluded that depression is not featured by mood-congruent biases in attention (association question), thereby contradicting predictions made by Beck's depression model (D. A. Clark et al., 1999). According to the reformulated model, depressed individuals engage in strategic or biased elaboration upon negative material during memory retrieval. This enhanced elaboration results in improved memory for similar information and, in addition, such elaborations can serve as mnemonic cues at later points in time (causal question).

Impaired Cognitive Control Accounts

There is growing interest into the cognitive mechanisms that operate across biases at various levels of information processing. The idea of executive control as an overarching mechanism has been proposed by several researchers (e.g., Hertel, 1997; Joormann, Yoon, et al., 2007). Interestingly, Joormann et al.'s impaired cognitive control account (2007; 2010) specifies a causal pathway linking deficits in cognitive control to cognitive biases (causal question). The impaired cognitive control account asserts that depressed individuals have difficulties in limiting the access of irrelevant negative information into working memory (WM) and removing negative content that is no longer relevant from WM. For example, negative cognitions about past failures that remain active in WM (e.g., "I failed my previous exam, why would I pass now") may interfere with the current performance on a task (e.g., when one is preparing for the next exam). It is hypothesized that such deficits in cognitive control underlie difficulties in disengaging attention from the processing of negative information. As a result, negative elaborations are stored into long-term memory, setting the stage for memory biases. Interestingly, whereas most cognitive frameworks predict schema-congruent biases that are determined by a higher-order factor (i.e., cognitive schemata; D. A. Clark et al., 1999; Ingram, 1984), Joormann et al. predict a cascade of biases that are driven by impaired cognitive control exerting an influence on attention and memory. It is clear that a different pattern of causal relations between cognitive processes is predicted by Joormann, Yoon, et al. (2007) compared with models of Beck (D. A. Clark et al., 1999), Ingram (1984) and Williams et al. (1988; 1997).

Summary

As discussed above cognitive theories differ in the extent they integrate multiple distorted aspects of information processing, elaborate on the interplay among such processes, and provide predictions regarding the possible ways in which cognitive biases can influence symptoms of depression in a collective manner. Thus, the CCBH can be applied to examine

the competing hypotheses arising from these different models. Yet, despite these meaningful core and differential predictions, the existing models are nevertheless ambiguous and underspecified as far as the dynamic interplay among cognitive biases is concerned. The sections below provide an overview of the current research reporting data informative about the CCBH.

Empirical Data on Combined Cognitive Biases

There are, as noted, an increasing number of studies investigating the interplay among attention, interpretation, and memory biases in depressed samples. Table 2 provides an overview of the published research to date.

Association Questions

An important line of studies testing associations between cognitive biases has focused on emotional biases in attention and explicit memory processes. A seminal study by Gotlib et al. (2004) explored the interplay between these processes in a sample of clinically depressed patients and never-disordered control individuals. All participants completed a self-referential encoding task in which the self-relevance of sad, angry, neutral, and happy words was evaluated, followed by an incidental free recall task to test memory for the presented words. Next, a dot probe task with emotional faces and an emotional Stroop task were administered. The dot probe task (MacLeod, Mathews, & Tata, 1986) is a measure of spatial attention which presents emotional-neutral stimulus pairs followed by a probe at the spatial location of one of these stimuli. Reaction times to the probe allow the inference of whether attention was allocated to the neutral or the emotional stimulus. The emotional Stroop (Stroop, 1992) displays negative and neutral words written in different colors and participants are asked to name the color of each word. Naming latencies reflect the interference between color naming and attention allocated to the semantic content. Although depressed individuals showed an attention bias for sad faces in the dot probe task and recalled more negative and fewer positive

words, no significant correlations emerged between the different bias indices. No biases in attentional interference emerged on the emotional Stroop task. These findings suggest that even when attention and memory biases were both present in the same population, they were not associated. However, the lack of convergence between the attention bias indices suggests that the dot probe and emotional Stroop task may not be tapping into the same underlying attention processes. It is also likely that in this study, the absence of strong interrelations among the different bias indices could have been due to the error variance associated with information processing tasks or incongruence in the type of stimuli used in each task (i.e., facial expressions vs. verbal stimuli).

Two recent studies in stable dysphoric samples provide some support for a relationship between biased attention and memory processes. A study by Koster, De Raedt, Leyman, and De Lissnyder (2010) investigated whether mood-congruent attention at different levels of elaboration is associated with memory biases. In a spatial cueing task (Posner, 1980) neutral and emotional cue words were presented in either the left or the right placeholder, and these were in turn followed by a target appearing in the same (i.e., valid trials) or opposite (i.e., invalid trials) placeholder as the emotional (or neutral) cue. By manipulating the cue target onset asynchrony (CTOA; i.e., the time between offset of cue and onset of target), it was possible to provide an index of the time course of attention on cue words. A subsequent incidental free recall task tested memory for the previously presented words. Results showed that dysphoric students demonstrated an attention bias for negative words only under conditions where the CTOA allowed for elaborate processing and, interestingly, this bias predicted the recall of negative words. Finally, this association remained significant even after controlling for the severity of depressive symptoms.

Further evidence to indicate that cognitive biases in depression are related to each other was reported by Ellis, Beevers, and Wells (2011) using eye-tracking methods.

Dysphoric and nondysphoric participants completed a naturalistic visual scanning task (Eizenman et al., 2003) in which gaze behavior was monitored while viewing a series of slides depicting dysphoric, aversive, neutral, and positive words. This task was followed by an incidental recognition task for the displayed words. The dysphoric group exhibited an absence of a positive attention bias (indexed by the percentage of time fixating on positive stimuli), and this predicted less accurate recognition of previously presented positive words.

Attentional breadth has also been studied in relation to explicit memory. For instance, Wells, Beevers, Robison, and Ellis (2010) presented dysphoric and nondysphoric undergraduates with a series of happy, sad, angry, and neutral facial expressions while recording their eye movements. An incidental recognition task assessed memory for the expressions. Analyses showed a broader attention focus for angry faces in dysphoric individuals compared with nondysphoric participants. This broader focus of attention was inferred from larger inter-fixation distances upon viewing the slides. The attentional breadth for angry faces was correlated with enhanced recognition for similar faces.

In sum, the current pattern of findings suggests that in dysphoric samples emotional distortions in attention and memory are related to each other. However, there is no evidence supporting this association in clinically depressed samples. We now turn to discussing research findings on the association between memory and interpretation biases in relation to the causal questions.

Causal Questions

The effects of self-focused attention. Several theoretical frameworks (e.g., Beck's cognitive model) have attributed a crucial role to attention towards self-relevant information in relation to other cognitive biases. To examine the effects of self-focused attention, studies have induced self-focus through thought-induction procedures (e.g., Nolen-Hoeksema & Morrow, 1993) which require participants to explore the meaning of a series of self-focused

and other-focused items (e.g., “my character and who I strive to be”, “the physical sensations in your body”). Two studies by Hertel and El-Messidi (2006) examined the effects of manipulating the focus of attention in relation to interpretation and memory biases. In the first experiment, focus of attention (self vs. other) was manipulated and participants completed an interpretation task in which they formed sentences with serially presented homographs (e.g., loaf, reflect). It was found that dysphoric individuals created more sentences revealing negative interpretations of the homographs in the self-focus than in the other-focus condition. The manipulation of attentional focus (self vs. other) did not directly affect the focus, namely personal vs. impersonal, of subsequently created sentences. However, there were significant correlations between negative and personal sentences. In a second study, participants were presented with homographs after the self-focus manipulation and their task was now to report the first words that came to mind. This was followed by an incidental free recall task testing memory for the homographs. Dysphoric individuals interpreted the homographs more often as personal and recalled more personally interpreted homographs in the self-focus than in the other-focus condition. Results of both studies suggest that heightened self-focused attention in dysphoric individuals may lead to more negative and personal interpretations of ambiguous information that may transfer to memory processes.

In a related manner, a study manipulated the focus of attention in depressed patients to investigate the consequences for autobiographical memory specificity (E. Watkins & Teasdale, 2004). Prior to the attention manipulation, participants were instructed to focus either on the experience described in each item (i.e. experiential condition) or on the causes and consequences of each item (i.e. analytical condition). An autobiographical memory test (Williams & Broadbent, 1986) was administered before and after the attention focus manipulation. This memory test asks participants to produce a specific personal memory in response to positive and negative cue words. It was found that depressed patients engaging in

an experiential self-focus (which is considered as adaptive) recalled less overgeneral memories after the manipulation procedure. The overgeneral memories persisted in depressed patients engaging in an analytical self-focus (a pathological variant of self-focus).

The findings of these studies collectively provide evidence for an association between attention, interpretation, and memory processes. It should be noted, however, that despite these interesting findings, inducing self-focus could influence other cognitive processes (e.g., self-critical thinking) that may have contributed to the results.

Interpretation biases and explicit memory. Two published studies have examined how induced negative and positive interpretation bias affect memory in unselected samples. A study by Salemink, Hertel, and Mackintosh (2010) investigated whether memory for prior ambiguous events changed by subsequently established interpretation biases. First, participants were presented with (to-be-remembered) ambiguous social scenarios and asked to generate a least one ending for the story. Next, either a positive or a negative interpretation bias was induced. In short, such modification procedures induce interpretation biases by presenting participants with a series of ambiguous stories each ending with a word fragment for participants to complete. This word fragment imposes either a positive or negative meaning on the ambiguous story (for details see Mathews & Mackintosh, 2000). Upon completion, participants completed an incidental cued recall task to test memory for the initial scenarios and their endings. Results showed that the interpretation training affected memory for endings of prior ambiguous scenarios in a training-congruent manner, with positively trained participants remembering the endings of the stories as more positive than negatively trained participants. No training-group differences emerged in recall of initial scenarios.

These results were extended by Tran, Hertel, and Joormann (2011). After a positive or negative interpretation bias training (procedure similar to Mathews & Mackintosh, 2000), ambiguous stories ending with a to-be-completed word fragment were presented to the

participants (encoding phase). Different from the training scenarios, completion of the fragments in the encoding phase did not disambiguate the story in a positive or negative manner. Next, memory for these ambiguous scenarios was tested in a recall task. It was found that induced positive and negative interpretation biases resulted in corresponding positive and negative memory biases. Taken together, these findings suggest that emotionally biased interpretation processes influence memory for to-be-encountered as well as memory for previously encountered information.

Predictive Magnitude Questions

At present, there is, to the best of our knowledge, only one study published investigating the predictive magnitude of multiple cognitive biases in a single study. In a follow-up of the major depressed patients recruited by Gotlib et al. (2004), it was examined whether the biases observed in attention (measured by a dot probe task) and memory (assessed by an incidental free recall task) predicted the course of depression (Johnson et al., 2007). Results showed that depressed patients who recalled a higher proportion of positive words at time one reported less severe symptoms nine months later. Furthermore, negative biases in neither attention nor memory related significantly to the change in depressive symptom severity. None of the cognitive biases predicted recovery from major depression. These findings suggest that even though different cognitive biases were present (i.e., attention and memory biases; cf. Gotlib et al., 2004), their effect on the prediction of depression was limited. Moreover, in the presence of multiple biases only some may have a predictive effect on depressive symptoms (e.g., memory biases), whereas others may not (e.g., attention biases).

Summary

The increasing number of studies on the interplay between cognitive biases has yielded some promising patterns of findings. First, there is evidence suggestive of significant

interrelations between depression-related biases in attention and explicit memory in dysphoric individuals (Ellis et al., 2011; Koster et al., 2010; Wells et al., 2010). In clinical depression, attention and memory biases may operate in isolation and differentially affect the course of depression (Gotlib et al., 2004; Johnson et al., 2007). Second, induced self-focused attention affects interpretation biases in dysphoria (experiment 1, Hertel & El-Messidi, 2006) and, moreover, analytical self-focus disturbs memory specificity in clinical depression (E. Watkins & Teasdale, 2004). Under conditions of heightened self-focus, distorted interpretations of ambiguous information transfer to memory (experiment 2, Hertel & El-Messidi, 2006). Third, acquired interpretation biases influence memory for past ambiguous information and memory for subsequently encountered information (Salemink et al., 2010; Tran et al., 2011).

In spite of the evidence on the relationship between cognitive biases, no research to date has examined how the relationship between various cognitive biases may be influenced by impairments in cognitive control. Given that cognitive control is hypothesized to be an overarching construct that could account for the observed relationships between cognitive biases in depression (e.g., Joormann, Yoon, et al., 2007), future research should investigate the modulating role of cognitive control impairments in relation to cognitive biases systematically. There is also a need to investigate the relationship between cognitive biases in a variety of samples, such as clinical or at-risk samples.

Theoretical and Clinical Considerations

Frameworks of Depression

Theoretical implications of current findings. Information processing models of depression are expected to consider the possible interactions between cognitive biases as the current data in general provides support for interrelations among emotionally biased cognitive processes. Several implications can be discussed. As predicted by most cognitive models (D. A. Clark et al., 1999; Ingram, 1984; Joormann, Yoon, et al., 2007; Williams et al., 1988),

current findings demonstrate interrelations among emotional distorted attention and congruent memory processes in samples of dysphoric individuals. More specifically, the reviewed data suggests that attention biases at later and not early processing stages are linked to congruent biases in explicit memory. These findings contradict predictions by Williams et al. (1997) that depression is not characterized by attention biases and are at odds with Beck's claim that biases emerge also at automatic levels of information processing (D. A. Clark et al., 1999).

In addition, the findings demonstrating that negative and positive interpretive biases are correlated with biases at the level of memory importantly suggest that biased information processing could contribute to the consolidation and elaboration of negative schema-content in memory (Ingram, 1984; Joormann, Yoon, et al., 2007; Williams et al., 1988, 1997).

However, it is not clear whether the elaborative processing of negative information can be attributed to the improved quality of encoding of negative information, as predicted by the enhanced elaboration accounts (Ingram, 1984; Williams et al., 1988), or to impairments in cognitive control, as predicted by Joormann, Yoon, et al. (2007). Taken together, biases in attention and interpretation may influence memory for emotional information, which is in line with the idea that cognitive biases maintain negative self-schemas in memory (D. A. Clark et al., 1999; Ingram, 1984). It is noteworthy that it is still unclear whether there are long-term influences of attention and interpretation on memory for emotional information.

As noted earlier, current studies in support of associations among cognitive biases have been conducted in nonclinical dysphoric samples and findings from the only published study examining attention and memory biases in clinical depression showed results inconsistent with data generated in dysphoric samples (cf. Gotlib et al., 2004). Thus, the present state of the literature only allows us to draw conclusions about dysphoric samples. Gotlib et al. (2004) used different stimulus material across tasks which may have reduced the

likelihood to find associations. Clearly, however, more work in clinically depressed samples is needed.

State vs. trait effects. As studies on the interplay between biased cognitive processes have been conducted in dysphoric and clinical depressed samples, it cannot be determined whether the observed interrelations are trait- or state-dependent effects of depression (i.e., cognitive schemata or mood). Although schema-congruent processing models of depression (D. A. Clark et al., 1999; Ingram, 1984) pose a direct impact of schemas on cognitive biases there is also evidence for effects of mood on negative cognitions and cognitive biases. For instance, a study examining diurnal mood variation in relation to autobiographical memories (D. M. Clark & Teasdale, 1982), found that depressed individuals were more likely to recall unhappy memories at times that are typically associated with more depressive complaints (e.g., mornings). This finding suggests that mood state effects are important in understanding the interplay between cognitive biases, as mood congruency effects might partially account for the observed interrelations between cognitive biases (besides trait factors such as cognitive schemas).

To disentangle state and trait effects, the interplay among processing biases can be studied in remitted depressed samples. Interestingly, in this regard, different cognitive formulations of depression predict that cognitive biases emerge only under certain conditions in this population. Schema-models (e.g., D. A. Clark et al., 1999; Ingram, 1984), for example, propose that after a depressive episode negative schemata remain latent but can be activated at any point in time by distressing situations (e.g., failing an exam). Consequently, remitted depressed individuals will not exhibit biases in attention, interpretation, and memory when not distressed. In contrast, the impaired cognitive control account (Joormann, Yoon, et al., 2007) does not specify that negative mood state is required to find biases as it asserts that cognitive biases operate as long as the cognitive control impairments persist. As several

studies demonstrate cognitive control impairments in formerly depressed individuals (see Joormann, 2010), biases and their interplay should also emerge without negative mood states according to the impaired cognitive control account. Further study of cognitive biases in remitted depressed individuals with and without negative mood would allow testing the differential predictions from these cognitive models.

Methodological considerations. A number of methodological issues seem relevant to the study of the combined cognitive bias hypothesis as introduced in this paper. The review of empirical studies on the combined cognitive biases demonstrate that present research has tested interrelations using primarily cross-sectional study designs that include only a limited set of cognitive processes, and have applied basic statistical techniques (e.g., correlational analysis) to analyze interrelations. Thorough examination of the CCBH requires statistical testing and modeling of direct and indirect links between multiple variables (e.g., cognitive biases) and constructs (e.g., negative schemata). This necessitates appropriate statistical methods. For example, structural equation modeling (Hoyle, 2012) can enable theory-driven tests of predictions using methods such as path analysis, structural regression models, and latent change models. Other data driven approaches (see Hsieh et al., 2011) allow for the investigation of interrelationships among multiple variables. Here information is obtained about the structure (i.e., associations among variables) and dynamics (i.e., clusters of variables) of the system in a stepwise manner starting from pairwise correlations among variables.

Another issue concerns the reliability of the experimental tasks developed or modified to study emotionally biased aspects of information processing in depression (for overviews see Harvey, Watkins, Mansell, & Shafran, 2004; Wenzel & Rubin, 2005). Remarkably, at present, data from studies examining psychometric properties are equivocally supportive for the reliability of experimental tasks used. For example, low split-half and test-retest

reliabilities as well as nonsignificant correlations between bias indices have been reported for different versions of the dot probe task (Salemink, van den Hout, & Kindt, 2007; Schmukle, 2005). Furthermore, it has been observed that bias indices intended to measure the same construct often do not correlate with each other. Gotlib et al. (2004), for example, found correlations close to zero between attention bias towards sad faces in a dot probe task and emotional Stroop scores (see also Dalglish et al., 2003; Mogg et al., 2000). This finding raises doubts over the convergent validity of these measures (but see Salemink and van den Hout (2010) and Griffith et al. (in press) who managed to find acceptable psychometric properties of their tasks). Clearly further empirical work is needed in this area.

A final issue that deserves consideration is the frequent medication use in the samples under investigation. Given that currently depressed participants in clinical studies often receive pharmacological treatment, effects of medication on mood and the interplay among cognitive biases needs to be taken into account. For instance, a study in a non-clinical sample observed that 7-days administration of citalopram, a selective reuptake inhibitor, produced enhanced memory for positive words (Browning et al., 2011). This illustrates that pharmacological interventions can have beneficial effects on cognitive biases, and possibly their interplay. As such, considering the influence of medication use is important.³

Predicting Depression

In the introduction of this article we argued that cognitive biases are not just an epiphenomenon of depression, but represent a vulnerability or latent endogenous process that is reactive to stress (Ingram & Siegle, 2009). Although empirical data from longitudinal studies have found that biases in attention (Beevers & Carver, 2003), interpretation (Rude, Durham-Fowler, Baum, Rooney, & Maestas, 2010; Rude et al., 2003; Rude et al., 2002), memory (Johnson et al., 2007; Sumner et al., 2010) and impairments in cognitive control (Zetsche & Joormann, 2011) can predict depressive symptoms and clinical depression, it is

notable that the obtained effects sizes are often small to moderate. In line with Mathews and MacLeod (2005) we believe that biased cognitive processes can have substantial effects on depression through their mutual interactions and interaction with stressful life events, affecting emotional reactivity to stress that may subsequently lead to depressive symptoms and episodes. Research on the combined influence of multiple cognitive biases on depressive symptoms is clearly still in its infancy. In this context, several broad issues should be taken into account, such as potential variations in the interplay between cognitive biases among stadia of the depression course, dysfunctional emotion regulation strategies through which multiple cognitive biases impact depressive symptoms, and biological vulnerability factors. These issues are discussed in turn.

Variations in the interplay. In examining the predictive value of cognitive biases, potential differences in the interplay between biases among different stadia in the course of depression should be taken into consideration. It seems plausible that cognitive biases and the interplay among them will not remain static over time. For instance, the experience of becoming and being depressed (e.g., increasing sad affect, negative cognitions) might affect the magnitude of one or more cognitive biases (e.g., memory). One could expect, for example, that the interplay between these biases will be stronger as the number of depressive episodes increases (see Teasdale & Barnard, 1993). Some research suggests that individual biases differ in function of depression severity. A study by Baert, De Raedt, and Koster (2010) directly compared the strength of attention biases in individuals reporting minimal, mild, and moderate to severe depressive symptoms. Results showed that maintained attention towards negative information was associated with moderate to severe depressive symptom levels. Moreover, it has been found that differences in cognitive control impairments depend on the depressed sample tested. Specifically, valence-specific deficits in cognitive control were observed in a dysphoric students sample (De Lissnyder, Koster, & De Raedt, In press),

whereas clinically depressed individuals showed only global cognitive control impairments (De Lissnyder et al., 2011). Taken together, future research will need to compare the interplay between cognitive biases across divergent samples corresponding with the stadia of the depression course (e.g., non/never-depressed at risk, clinically, and remitted depressed) to increase our understanding of cognitive vulnerability for depression.

Emotion regulation strategies. The present research has generally focused on cognitive biases in relation to emotional reactivity and depressive symptoms (e.g., sustained negative affect). However, it remains unclear whether cognitive biases, and in particular their interplay, have direct effects on depressive symptoms or whether this relationship is mediated by other cognitive processes such as maladaptive emotion regulation strategies (e.g., rumination). In line with the latter view, it has been argued, for example, that cognitive control deficits underlie the reduced ability to use strategies (e.g., use positive autobiographical memories, reappraisal) to regulate sad mood in depression (e.g., De Raedt & Koster, 2010; Joormann & D'Avanzato, 2010). There is emerging research testing this hypothesis. For instance, prospective studies have observed that cognitive control impairments predict later depressive symptoms in non-clinical samples (Zetsche & Joormann, 2011) and, in remitted depressed individuals, the relationship between cognitive control and depressive symptom levels is fully mediated by rumination (Demeyer, De Lissnyder, Koster, & De Raedt, 2012). In sum, the mechanisms by which cognitive biases and their interplay relate to emotion regulation strategies and depressive symptoms provide a fruitful avenue for future research.

Biological vulnerability factors. Biased cognitive processes are expected to interact with genetic and neurobiological vulnerability factors (e.g., De Raedt & Koster, 2010). Genetic risk factors, such as variations in the serotonin transporter gene (5-HTTLPR), are associated with vulnerability for depression through their effects on social cognition

(Homberg & Lesch, 2011). More specifically, it is argued that genetic factors are associated with higher levels of vigilance for signs of social threat, which has been found both at the neurobiological levels (e.g., enhanced amygdala activity on presentation of fearful faces; Hariri et al., 2005) and cognition (Beevers, Gibb, McGeary, & Miller, 2007). In addition, genetic factors in interaction with stressors have been linked to reactivity in neural substrates (Caspi & Moffitt, 2006) with, interestingly, a correspondence between abnormalities at the neural system level and distortions in cognitive processes observed in depressed samples (De Raedt & Koster, 2010). For instance, it has been found that upon encountering negative material the increased activation in limbic regions (e.g., amygdala, hippocampus) is related to a reduced activity in specific regions in the prefrontal cortex (e.g., dorsolateral prefrontal cortex, orbitofrontal cortex, anterior cingulate cortex) with these latter structures being crucial to implement cognitive control over processing of affective material (Davidson et al., 2002; Whittle, Allen, Lubman, & Yucel, 2006). The emerging integrative (gene-by-environment) views on depression allow further exploration of the interplay among genes, neuroendocrine, and stress in relation to multiple cognitive biases (Disner, Beevers, Haigh, & Beck, 2011).

Modification of Cognitive Biases

Given the specific challenges in the treatment of depression, it is important to consider the current findings on the CCBH in light of therapeutic interventions for depression. Extant data showing associations among different aspects of depressogenic information processing may indicate that these biases in concert can play an important maintaining role in depressive complaints. In many psychological treatments of depression, a main aim is the modification of underlying negative schemas (D. A. Clark et al., 1999). However, when individuals are severely depressed, cognitive biases may hamper the effectiveness of verbal information transmission due to concentration, attention, and memory impairments. Moreover, emotion-specific biases can strongly counteract therapeutic interventions as the encoding and

elaboration of information is strongly favored towards schema-congruent information (Baert, Koster, & De Raedt, 2011).

CCBH and improving cognitive training. Given the maintaining role of information processing biases, it is important to consider the potential value of targeted cognitive training that can either train neural structures known to be impaired in depression (Siegle et al., 2007) or modify emotion specific biases in attention (Baert, De Raedt, Schacht, & Koster, 2010; Wells & Beevers, 2010), interpretation (Blackwell & Holmes, 2010; Holmes, Lang, & Shah, 2009; Lang, Blackwell, Harmer, Davison, & Holmes, 2011) or memory (Joormann, Hertel, LeMoult, & Gotlib, 2009; Raes et al., 2009). In general, cognitive bias modification (CBM) methodologies target specific cognitive processes by exposing participants to experimentally established contingencies during a task designed to encourage the acquisition or attenuation of an information processing bias (Koster, Fox, & MacLeod, 2009). Notwithstanding promising findings, the number of CBM studies in depression needs to be extended and enlarged (see MacLeod, Koster, & Fox, 2009). At this point, further refinement of CBM procedures, and especially their implementation in clinical practice, can benefit from better insights gained through studies investigating the CCBH. If, for example, the impact of a certain cognitive bias on other biases and depressive symptoms differs depending on the depression phase, the preferred CBM intervention should be chosen accordingly. Moreover, depending on the precise interplay among cognitive biases in depression (e.g., unidirectional, bidirectional effects), the optimal training program might not only depend on the targeted aspect of information processing (i.e., attention, interpretation, memory, cognitive control) but also on the number of targeted cognitive biases. For instance, if various biases operate in a reciprocal manner, one might have to train multiple biases simultaneously to efficiently obtain clinically significant and enduring symptomatic improvement. In this regard, some promising findings were reported in a pilot study combining attention and interpretation bias training in clinical

anxious outpatients (Brosan, Hoppitt, Shelfer, Sillence, & Mackintosh, 2011). A reduction in attention and interpretation biases was observed together with a decrease in trait and state anxiety. Clearly, research on the CCBH provides promising implications for future CBM applications.

As these training methodologies find their way to clinical practice, they will generally be combined with other approaches to modifying biases (e.g., pharmacological interventions). Note that different interventions may change biases for emotional information through distinct mechanisms (see Browning, Holmes, & Harmer, 2010) and, moreover, may not always interact in the predicted way as is reflected by the outcome measures. For instance, a study examining effects of citalopram combined with attention bias modification in healthy participants, found that the combined interventions were less effective in inducing a positive bias than each individual intervention (Browning et al., 2011). This warrants specific research on the processes underlying training methodologies to optimize combinations of treatment strategies.

CCBH and mechanisms underlying CBM. Providing inspiring directions for future research, Hertel and Mathews (2011) discuss the automatic and controlled processes involved in CBM procedures and correctly stress the relevance of learning principles (i.e., classical and operant conditioning) and memory research in understanding how cognitive bias training works. Besides clinical implications of knowledge about underlying processes of cognitive training, it is also of crucial importance for CCBH research to examine the precise mechanisms underlying CBM through training, as this is an important way to be as specific as possible in addressing the “causal question” of the CCBH.

Conclusion

In this review, we have argued for an approach that considers the interplay between cognitive biases. Based on empirical findings, we have shown that an association between

different depression-related cognitive biases. This indicates that the relations and effects of cognitive biases should be studied in a more integrative manner. The overview also showed that research on this topic is still in its infancy. Future research in this domain may be guided by the outlined types of unanswered questions originating from the CCBH and their integration with distinct cognitive frameworks of depression providing specific predictions on the interplay among cognitive biases. Arguably, our understanding of depression and thereby clinical practice will only benefit from scientific research that directly examines the links between biased cognitive processes identified in depression. With this review, we hope to stimulate future research on the CCBH in depression.

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Footnotes

¹ The terms cognitive biases, distorted cognitive processes, and information processing biases are used interchangeably and denote biases in attention, interpretation, memory, and cognitive control processes.

² Note that this overview of cognitive frameworks is not exhaustive and presents only depression-specific models on cognitive biases that have guided empirical research on single cognitive biases in depressed samples.

³ The discussion of potential influences of medication on the interplay among cognitive biases is beyond the scope of this review.

Table 1

CCBH Research Questions

Type	Key features
Association questions	Research questions concern whether cognitive control impairments, attention, interpretation and memory biases are associated.
Causal questions	Hypothesized causal relations among cognitive biases are of central interest. Research questions concern whether associated information processing biases operate in succession with unidirectional influences, in parallel without mutual influences, or in a reciprocal manner.
Predictive magnitude questions	Questions involve the effects of cognitive biases in concert vs. in isolation on the depression course. Addressing whether additive and/or interactive effects of cognitive biases on depressive symptoms extend beyond biases' isolated effect is central to this type of questions.

Table 2

Empirical Studies on the CCBH

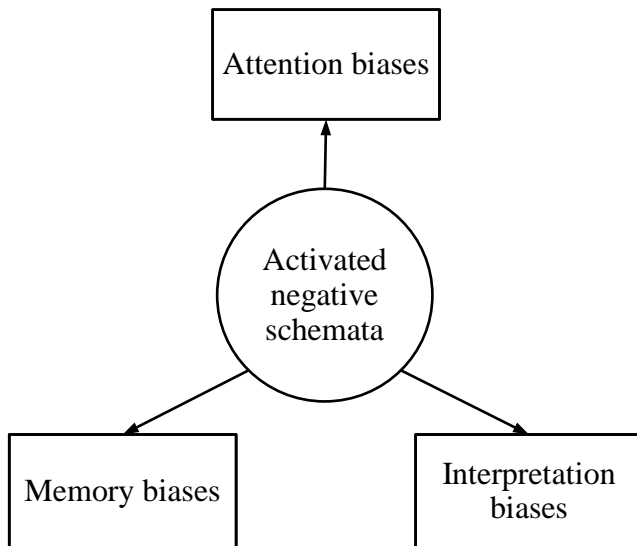
Study	Sample	Findings
<i>Association questions</i>		
Gotlib et al. (2004)	Clinical depressed patients, never-disordered adults	No significant correlations between observed attention and explicit memory biases
Koster et al. (2010)	Stable dysphoric and non-dysphoric undergraduate students	Negative attention bias at the later processing stages predicts recall of negative words in dysphoric students
Ellis et al. (2011)	Stable dysphoric and non-dysphoric undergraduate students	Absence of positive attention bias predicts less accurate recognition of positive words
Wells et al. (2010)	Stable dysphoric and non-dysphoric undergraduate students	Greater attentional breadth for angry stimuli predicts enhanced recognition of similar facial expressions
<i>Causal questions</i>		
Hertel and El-Messidi (2006; experiment 1)	Dysphoric and non-dysphoric undergraduate students	Dysphoric participants make more negative interpretations under increased self-focused attention
Hertel and El-Messidi (2006; experiment 2)	Dysphoric and non-dysphoric undergraduate students	Under heightened self-focused attention dysphoric individuals interpret more homographs as personal which are subsequently recalled to an increased extent
E. Watkins and Teasdale (2004)	Clinical depressed patients	Overgeneral memories persisted under analytical self-focus, whereas non-analytical self-focus decreases overgeneral memories

Table 2

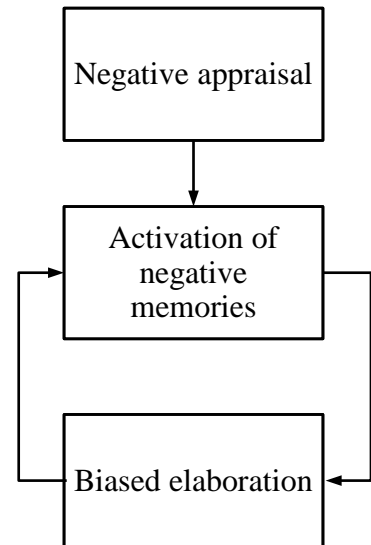
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Study	Sample	Findings
Salemink et al. (2010)	Unselected undergraduate students	Established interpretation biases affect memory for previously encountered information.
Tran et al. (2011)	Unselected undergraduate students	Established interpretation biases influence memory for subsequently encountered information.
<i>Predictive magnitude questions</i>		
Johnson et al. (2007)	Clinical depressed patients, never-disordered adults	<p>Number of recalled positive words predicts symptomatic change nine months later.</p> <p>Neither negative memory nor attention biases indices were related to changes in symptom severity. No bias indices predicted recovery from depression.</p>

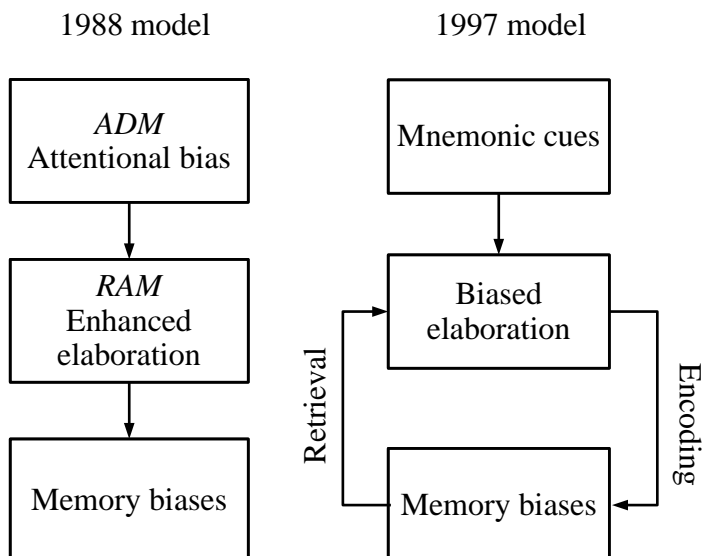
(a) Beck's schema model



(b) Ingram's information processing analysis



(c) Frameworks of Williams, Watts, MacLeod and Mathews



(d) Impaired cognitive control account (Joormann et al., 2007)

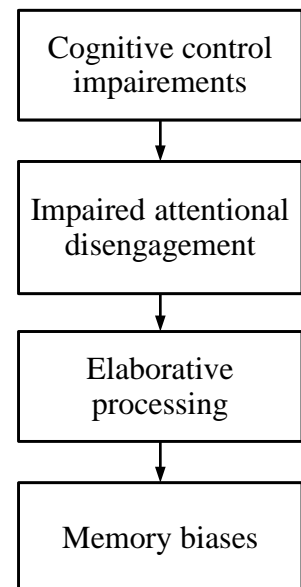


Figure 1. Schematic Depiction of Interrelations Among Cognitive Biases According to Cognitive Frameworks of Depression.